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61750-142

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#13 Decl

Application of	:	BAZIN, *et al.*
Serial No.	:	08/472,281
Filed:	:	JUNE 7, 1995
For	:	LO-CD2A ANTIBODY AND USES THEREOF FOR INHIBITING T CELL ACTIVATION AND PROLIFERATION
Group	:	1816
Examiner	:	Gambel, P.
Our File No.	:	61750-142

Assistant Commissioner of Patents
Washington, D.C. 20231

DECLARATION

Sir:

Mary White-Scharf declares as follows:

1. My C.V. is attached as Exhibit 1.

2. I am familiar with the referenced application, certain work performed with respect to LO-CD2a, and the prior art relied on by the Examiner.

3. I was also present at the recent interview with the Examiner in which he requested information with respect to whether or not work had been performed to ascertain whether or not LO-CD2a bound to an epitope which differed from other CD2 antibodies.

4. Peterson *et al.* (Nature 329, 842-46 (1987) (copy attached)) developed a procedure for epitope mapping of CD2 antibodies. In brief, the procedure involves preparing CD2 mutants wherein one or more amino acids of CD2 are mutated. CD2 antibodies are then tested against a panel of the CD2 mutants to determine which amino acid mutation(s) affect CD2 antibody binding. If an antibody does not bind to a CD2 mutant, then the amino acid(s) which has been mutated determines the epitope for such antibody.

5. Peterson *et al.* used the procedure for mapping the epitope for a plurality of CD2 antibodies.

6. The LO-CD2a antibody of the present application was tested against CD2 mutants of Peterson *et al.* to ascertain whether or not LO-CD2a would bind to CD2 mutants as to which binding was lost for known CD2 antibodies. If LO-CD2a were bound by such CD2 mutants, then LO-CD2a bound to an epitope which differed from the epitope for the antibody which did not bind to such mutant.

7. For the following CD2 antibodies reported by Peterson *et al.*, LO-CD2a bound to a mutant as to which there was a loss of binding for such CD2 antibody, thereby indicating that the epitope for LO-CD2a differed from the epitope for each of such antibodies.

8. The results are as follows:

(a) As reported by Peterson *et al.*, Antibody 9.6 - did not bind when amino acid, 46, 48 or 51 was mutated. LO-CD2a bound to each of these mutants.

(b) As reported by Peterson *et al.*, Antibody 7E10 - did not bind when amino acid 48 or 51 was mutated. LO-CD2a bound to each of these mutants.

(c) As reported by Peterson *et al.*, Antibody MT 110 - did not bind when amino acid 48 was mutated. LO-CD2a bound to this mutant.

(d) As reported by Peterson *et al.*, Antibody MT 910 - did not bind when amino acid 48 was mutated. LO-CD2a bound to this mutant.

(e) As reported by Peterson *et al.*, Antibody MT 95 - 5 - 49 - did not bind when amino acid 48 or 51 was mutated. LO-CD2a bound to each of these mutants.

(f) As reported by Peterson *et al.*, Antibody T 11/3PT2H9 - did not bind when amino acid 51 was mutated. LO-CD2a bound to this mutant.

(g) As reported by Peterson *et al.*, Antibody 35.1 - did not bind when amino acid 51 was mutated. LO-CD2a bound to this mutant.

(h) As reported by Peterson *et al.*, Antibody 9.2 - did not bind when amino acid 48 or 51 was mutated. LO-CD2a bound to this mutant.

(i) As reported by Peterson *et al.*, Antibody T 11/3T4 - 8B5 - did not bind when amino acid 91 was mutated. LO-CD2a bound to this mutant.

(j) As reported by Peterson *et al.*, Antibody Nu-TER - did not bind when amino acid 92 or 99 was mutated. LO-CD2a bound to each of these mutants.

(k) As reported by Peterson *et al.*, Antibody CLBN-T11/1 - did not bind when amino acid 91 or 99 was mutated. LO-CD2a bound to each of these mutants.

(l) As reported by Peterson *et al.*, Antibody 39 B 21 - did not bind when amino acid 91 or 99 was mutated. LO-CD2a bound to each of these mutants.

(m) As reported by Peterson *et al.*, Antibody F 92 - 3A11 - did not bind when amino acid 91 was mutated. LO-CD2a bound to this mutant.

(n) As reported by Peterson *et al.*, Antibody F 9-1 - did not bind when amino acid 140 and 141 was mutated. LO-CD2a bound to this mutant.

(o) As reported by Peterson *et al.*, Antibody OCH.217 - did not bind when amino acid 140 and 141 was mutated. LO-CD2a bound to this mutant.

9. I have reviewed Xia *et al.* (Rat Monoclonal Antibodies Specific for Human T Lymphocytes) and in my opinion Xia *et al.* does not provide sufficient information to enable one skilled in the art to obtain the LO-CD2a antibody referred to therein.

10. Xia *et al.* provides a generic procedure for producing T-cell antibodies, and such procedure would not specifically produce LO-CD2a. Instead, such procedure would produce a variety of T-cell antibodies, including a variety of CD2 antibodies.

11. Xia *et al.* provides data as to the reactivity of the produced antibodies with a variety of cell lines which are known to include T-cell antigens.

12. The Xia *et al.* data are typical of data presented in scientific papers with respect to binding patterns of T-cell antibodies; however, reported data of this type are not accepted in the art as being suitable for identifying whether or not an antibody produced by a generic

procedure of the type described by Xia *et al.* is the same as an antibody previously reported in the literature.

13. The data reported by Xia *et al.* are obtained by cell based assays. As a result of the known variability in cell based assays of the type described by Xia *et al.*, one skilled in the art would not expect that a repetition of such assays would produce similar results. Thus, such assays are not reliable for uniquely identifying a specific antibody.

14. The data which is generally accepted in the art for determining whether or not two antibodies are the same antibody is data directed to epitope binding and/or binding inhibition.

15. Xia *et al.* provides no information with respect to binding inhibition or epitope binding and, therefore, one skilled in the art would not be able to ascertain whether or not an antibody produced by the generic procedure described by Xia *et al.* was LO-CD2a. In other words, in the absence of data with respect to epitope binding and/or binding inhibition, there is no practical way of determining from the data presented by Xia *et al.* whether or not an antibody produced by the generic procedure of Xia *et al.* is LO-CD2a.

16. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

DATE: 12/3/96

MARY WHITE-SCHARF

I hereby certify this correspondence is being deposited with the United States Postal Service first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on 12/13/96
(Date of Deposit)

Elliot M. Olstein
Name of applicant, Assignee, or Registered Representative

Elliot M. Olstein
Signature

12/13/96
Date of Signature